PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	School closures and influenza: systematic review of epidemiological studies
AUTHORS	Jackson, Charlotte; Vynnycky, Emilia; Hawker, Jeremy; Olowokure, Babatunde; mangtani, punam

VERSION 1 - REVIEW

REVIEWER	Sherry Towers Research Professor Arizona State University Tempe, AZ, USA
REVIEW RETURNED	05-Nov-2012

THE STUDY	The authors do not clearly discuss the criteria for exclusion of manuscripts. In addition, manuscripts were included that appear to be inappropriate for inclusion. The authors do not present a clear metric for what conclusions they wished to draw from the aggregated data. As a statistician, I found the statistical methods used to be questionable.
RESULTS & CONCLUSIONS	The paper does not provide any insights into the effect of school closures on influenza epidemics/pandemics that have not been presented elsewhere.
GENERAL COMMENTS	This manuscript summarizes several dozen studies of epidemic incidence before, after, or during school closures. As a document that summarizes such studies, and includes data from the 2009 pandemic, the work has some value, but it is not clear to me that it warrants publication in BMJ. I have several concerns about the paper. To begin with, Figures 1 and 2 show the inclusion of data from some papers with very questionable applicability to the topic. For instance, several histograms in Figure 1 show the number of children absent over time in various schools; during school closures, the number of children “absent” is shown as zero. This is not evidence of decreased incidence in an epidemic curve, as suggested by the Figure caption. There were no children listed as “absent” because the schools were closed. In Figure 2 there is one plot with only three data points, and one with only 5 (consisting again of cases counted within a school), and the school closure for the summer occurring at the very end, with zero counts (because the school was closed). The criteria used to determine which papers were to be included/excluded was not clearly presented. The authors ignore seasonality entirely, ascribing the widespread Northern Hemisphere reduction in summer incidence during the 2009 pandemic to school holiday closures. It is well known that temperature and humidity play a significant role in the seasonality of

	influenza, and that alone may account for the significant dip in summer incidence. Modeling studies have also shown that the seasonality of influenza in temperate climates can cause a pandemic to become much larger if a school closure is ill timed. The authors fail to mention a very key observation during the 1918 epidemic that death rates were lower in Connecticut towns that did not close schools compared to Connecticut towns that did close schools (http://www.ncbi.nlm.nih.gov/pubmed/22901071) The summary of the paper does not present any information that has not already been well covered in various seminal papers on this topic. It is already well know that school closures can potentially reduce transmission during an influenza outbreak. It is also known that optimal school closure strategies are unclear.

REVIEWER	Joseph Wu Associate Professor School of Public Health The University of Hong Kong I do not have any competing interests
REVIEW RETURNED	08-Nov-2012

GENERAL COMMENTS	The authors performed a nice systematic review of studies on the effect of school closure on reducing influenza transmission. I recommend acceptance after the following points have been addressed: 1. The authors indicated that this review extended previous reviews on the same topic by including new studies of the 2009 influenza pandemic. As such, the authors should point out more clearly on whether or how the new data from 2009 have helped us gain a better understanding of the effect of school closure on influenza transmission. 2. Presumably, the effect of school closure is larger for younger schoolchildren (i.e. kindergarten and primary schools) than older schoolchildren (i.e. high schools) because the latter are more likely to interact with their classmates in non-school settings during school closure. The authors should consider incorporating this factor into the results or discussions.

VERSION 1 – AUTHOR RESPONSE

Reviewer: Sherry Towers

The authors do not clearly discuss the criteria for exclusion of manuscripts. In addition, manuscripts were included that appear to be inappropriate for inclusion. The authors do not present a clear metric for what conclusions they wished to draw from the aggregated data. As a statistician, I found the statistical methods used to be questionable.

To reduce the potential for a biased conclusion, we did not exclude studies if no effect was seen but examine each of them to provide a full picture of the evidence regarding the effect of school closures

on influenza epidemics. The data available did not lend themselves to formal statistical summaries, hence the descriptive nature of the review. The great difficulty with identifying statistical metrics summarising the impact of school closures is reinforced by the fact that other high profile literature reviews on the same topic 1 2 also did not present summary metrics.

We realise though that the paragraph describing inclusion and exclusion criteria could be clarified, and it now reads as follows:
"Studies were included if they described one or more influenza outbreaks during which schools were initially open and subsequently closed, with or without other interventions. If papers presented several measures of influenza activity, the most specific data were extracted (e.g. data on laboratory-confirmed influenza were extracted in preference to all-cause school absenteeism). Studies which used modelling techniques to assess how school closure affected transmission based on real epidemic curves were eligible; however, predictive modelling studies exploring how school closure might affect a hypothetical outbreak were excluded. English translations (where available) of the titles and abstracts of papers written in other languages were screened, but these papers were not eligible for inclusion. Studies of outbreaks which started during school closure were excluded."

Although some of the papers which were eligible for inclusion provide limited useful information, we drew together as much data as possible on outbreaks which coincided with school closure, to provide an overview of the strategies used and the apparent effects on incidence / transmission.

We acknowledge that this is not a highly quantitative review and we have clarified this in the aims and objectives (the section "Data analysis" now begins "We summarised the data graphically and descriptively"). The data (epidemic curves with dates of school closure) were not expected to be amenable to meta-analysis and so we summarise the results descriptively.

The paper does not provide any insights into the effect of school closures on influenza epidemics/pandemics that have not been presented elsewhere.
Although our conclusions regarding the effects of school closure do not differ strongly from those of previous reviews (e.g. the Cauchemez paper in Lancet Infectious Diseases 1), we believe that it is worthwhile to summarise the additional data which have become available since that review was published, some of which strengthen the support for those conclusions. This provides a fuller summary of the evidence for public health agencies responsible for pandemic planning. We also now emphasise the information available from 2009 which has not been summarised before, as also suggested by the second reviewer (please also see our response to Joseph Wu's comments below).

This manuscript summarizes several dozen studies of epidemic incidence before, after, or during school closures. As a document that summarizes such studies, and includes data from the 2009 pandemic, the work has some value, but it is not clear to me that it warrants publication in BMJ.
Please see our response above.

I have several concerns about the paper.
To begin with, Figures 1 and 2 show the inclusion of data from some papers with very questionable applicability to the topic. For instance, several histograms in Figure 1 show the number of children absent over time in various schools; during school closures, the number of children "absent" is shown as zero. This is not evidence of decreased incidence in an epidemic curve, as suggested by the Figure caption. There were no children listed as "absent" because the schools were closed.
We assume this refers to the figures in the Supplementary Information. The figures here are intended only to present the data in order to put the main text into context. The captions do not imply that any apparent reductions in transmission are a result of school closure; for example the caption to

Supplementary Figure 1 is "Epidemic curves for seasonal influenza. Horizontal lines show periods of school closure (weekends are shown only if they are continuous with periods of pro-active or reactive closure). Data are daily unless the x axis indicates otherwise. See Supplementary Table 1 for case definitions and full details of the datasets."

School absenteeism data are labelled as such on the respective figures; we have now also marked each of these datasets with an asterisk on the epidemic curves. We hope that readers will be aware that that the reported zero absenteeism during school closure is not because of a reduction in transmission but that these data show whether the number of absences (or rate of absenteeism) is lower when schools reopen than might be expected based on the pre-closure absenteeism levels.

In Figure 2 there is one plot with only three data points, and one with only 5 (consisting again of cases counted within a school), and the school closure for the summer occurring at the very end, with zero counts (because the school was closed).
As stated above, we agree that some of the datasets are much less informative than others. However, as this is a systematic review we have provided the available information for all studies.

The criteria used to determine which papers were to be included/excluded was not clearly presented.
We have edited the paragraph which describes these criteria (please see response to comment above).

The authors ignore seasonality entirely, ascribing the widespread Northern Hemisphere reduction in summer incidence during the 2009 pandemic to school holiday closures. It is well known that temperature and humidity play a significant role in the seasonality of influenza, and that alone may account for the significant dip in summer incidence. Modeling studies have also shown that the seasonality of influenza in temperate climates can cause a pandemic to become much larger if a school closure is ill timed.
Thank you for this comment. Some of the included papers assessed the role of meteorological variables in mediating transmission of pandemic H1N1; others specifically studied the effects of empirically measured changes in contact patterns. We have added the following paragraph to the Discussion:

"Influenza transmission is influenced by factors besides contact in schools, including temperature and absolute humidity (AH) 3-6. Two studies which assessed the role of AH during the 2009 pandemic did not find strong evidence that it affected transmission 7 8. The two waves seen in the UK in 2009 could be explained by changes in contact patterns during school holidays 9 10. In a modelling study of data from Alberta, Canada, the best-fitting model included effects of temperature and school holidays on transmission, and predicted that if schools had not closed, the outbreak would have been restricted by temperature effects but would still have been 2.1 times larger than was observed in the province as a whole (1.38 and 1.54 times in the cities of Calgary and Edmonton, respectively) 11. A study of the interplay between school calendars, AH and population susceptibility in enhancing influenza transmission concluded that high AH may prevent influenza outbreaks 4. However, if a sufficiently high proportion of the population is susceptible, outbreaks can occur even when AH is high; the opening of schools may enhance transmission 4. Taken together, these studies suggest that contact in schools is not the only determinant of influenza transmission, but it is one influential (and modifiable) factor."

The authors fail to mention a very key observation during the 1918 epidemic that death rates were lower in Connecticut towns that did not close schools compared to Connecticut towns that did close schools (http://www.ncbi.nlm.nih.gov/pubmed/22901071)
Thank you for pointing this out. We now include a contemporary paper reporting this comparison 12 in

the review. In the section "Description of the epidemics" we now say "In Connecticut in 1918, three cities which closed schools experienced higher mortality rates than two which did not 12." This paper also raises the issue of reverse causality, which we now mention in the Discussion: "As noted in a study of the 1918 pandemic in Connecticut, reverse causality may occur when comparing rates in cities which closed schools to those in cities which did not, if closure was a response to a particularly severe local outbreak 12."

We have also updated Table 1, Figure 1 and Supplementary Table 2 accordingly.

The summary of the paper does not present any information that has not already been well covered in various seminal papers on this topic. It is already well know that school closures can potentially reduce transmission during an influenza outbreak. It is also known that optimal school closure strategies are unclear.
We agree that the conclusions are similar to those of previous reviews. However, we believe that an updated systematic review of the epidemiological evidence is helpful for informing policy regarding the response to pandemic influenza. We also consider it important to collate the additional data which have become available since those reviews were published.

Reviewer: Joseph Wu

The authors performed a nice systematic review of studies on the effect of school closure on reducing influenza transmission. I recommend acceptance after the following points have been addressed:

1. The authors indicated that this review extended previous reviews on the same topic by including new studies of the 2009 influenza pandemic. As such, the authors should point out more clearly on whether or how the new data from 2009 have helped us gain a better understanding of the effect of school closure on influenza transmission.
Thank you for this comment. We have added the following paragraph to the Discussion:

"In 2009, several countries closed schools whilst in others, planned holidays coincided with outbreaks. Several datasets from this pandemic strengthen support for school closure as an intervention; however, others illustrate that benefits are not guaranteed and that timely closure may be challenging. The sensitivity of the 2009 pandemic to school closures probably reflects the age-specific attack rates, which were higher in children than adults; outbreaks in which children are less affected might be less sensitive to school closure."

2. Presumably, the effect of school closure is larger for younger schoolchildren (i.e. kindergarten and primary schools) than older schoolchildren (i.e. high schools) because the latter are more likely to interact with their classmates in non-school settings during school closure. The authors should consider incorporating this factor into the results or discussions.
Thank you for this suggestion. Unfortunately the data identified do not allow comparisons of the effects of school closures on transmission in specific child age groups; however we agree that this is an important point and we have added the following to the Discussion:

"Studies presenting age-stratified data suggested that the effects of school closure on transmission were greater amongst children than adults. Few studies stratified children further, e.g. into primary and secondary school students. Older children might socialise more than younger children during school closures, so closing primary schools may have a greater effect on transmission than closing secondary schools (e.g. in Hong Kong in 2009, primary schools were closed pro-actively whilst secondary schools closed if cases occurred amongst their students 13)."

References
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VERSION 2 – REVIEW

REVIEWER	Sherry Towers Research Professor Arizona State University USA
REVIEW RETURNED	02-Jan-2013

THE STUDY	The stated aim of this paper is to review previous papers describing the effect of school closures on the spread of seasonal and pandemic influenza. There have been other comprehensive, well-written review studies that have examined the effect of school closures on pandemic and seasonal flu epidemics up to 2009. Most of the papers reviewed in this manuscript involve data from the 2009 pandemic, however this paper does not summarize what more was learned from the 2009 pandemic than was known before. A "review" paper of prior literature normally involves a summary of previous findings. This manuscript for the most part does not do that.
RESULTS & CONCLUSIONS	In my opinion this paper is not what I would consider to be a review paper, because it does not summarize previous findings with the purpose of gleaning and summarizing information from the

	combined body of previous literature. Instead, in my opinion, the manuscript is probably best described as an annotated bibliography of previous results.
GENERAL COMMENTS	This manuscript does not state or clearly define how it furthers the body of knowledge regarding the effect of school closures on the spread of influenza. As before, I recommend rejection of this manuscript because I do not feel that an annotated bibliography that does not summarize or interpret prior results is something that I personally consider to be worthy of publication.

VERSION 2 – AUTHOR RESPONSE

Reviewer: Sherry Towers
Research Professor
Arizona State University
USA

The stated aim of this paper is to review previous papers describing the effect of school closures on the spread of seasonal and pandemic influenza. There have been other comprehensive, well-written review studies that have examined the effect of school closures on pandemic and seasonal flu epidemics up to 2009.
Most of the papers reviewed in this manuscript involve data from the 2009 pandemic, however this paper does not summarize what more was learned from the 2009 pandemic than was known before. A "review" paper of prior literature normally involves a summary of previous findings. This manuscript for the most part does not do that.

In my opinion this paper is not what I would consider to be a review paper, because it does not summarize previous findings with the purpose of gleaning and summarizing information from the combined body of previous literature. Instead, in my opinion, the manuscript is probably best described as an annotated bibliography of previous results.

This manuscript does not state or clearly define how it furthers the body of knowledge regarding the effect of school closures on the spread of influenza. As before, I recommend rejection of this manuscript because I do not feel that an annotated bibliography that does not summarize or interpret prior results is something that I personally consider to be worthy of publication.

We note Professor Towers' comments. Whilst we acknowledge that our conclusions are similar to those of previous reviews, we consider it worthwhile to integrate the additional data from the 2009 pandemic with the previously available data. Some of this new information strengthens the evidence that school closure can reduce transmission, although important limitations remain in the evidence base (e.g. the optimum timing and duration of closure are unclear). We consider such an updated summary to be useful for formulating school closure policy in the event of a future pandemic, a severe seasonal outbreak or the emergence of a novel respiratory pathogen.